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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,109	08/01/2003	Kalev Kask	AGYT-017CIP2	3629

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/633,109	KASK ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/22/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I in the reply filed on 2/22/06 is acknowledged. Claims 1-13 are pending and under consideration.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1 .67(a) identifying this application by application number and filing date is required. See MPEP § 602.01 and 602.02. The oath or declaration is defective because the date of execution is missing.

Information Disclosure Statement (IDS)

3. Part of the information disclosure statement filed indicates that it is meant for another related application (10/246, 837). See application information in the upper right hand corner of pages 1-3 of 3 of the IDS submitted 1/13/04 by applicant. The examiner has considered the IDS in anticipation that Applicant has submitted it for the Examiner's consideration in the instant application.

Claim Objections

4. Claim 3 is objected to for minor informalities. Claim 3 ends in a sentence fragment with no period. A claim must consist of a single sentence only. Correction is required.

5. Claims 8-13 are rejected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The method of claim 1 identifies the agents of claims 8-13. Therefore claims 8-13 merely recite inherent characteristics of the method of claim 1.

Obvious Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harrasment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.32 1(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1. 130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-8, and 11-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3,

and 4 of US patent number 6, 521,414. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method to identify a modulator of NMDA receptor activity by detecting the ability of an agent to modulate tyrosine phosphatase activity. Claim 1 recites modulating 'a protein tyrosine phosphatase activity,' which is reasonably how claim I of the '414 patent functions (i.e., by identifying modulators of PTP1). The specification provides no distinguishing definition of 'on a substrate' or 'a substrate,' and systematically interprets ' a substrate' as a target of phosphatases or kinase, of which the NMDA receptor is known to be. Therefore the '414 patent meets the limitations of claim 1. Claims 3 and 4 are directed to method of measuring activity or binding, which are also recited directly, or are within the scope of the variations recited in claims 5 and 6 of the instant application. Claim 5 and 6 of the instant application is anticipated by claims 3 and 4 of the '414 patent. Claim 5 of the '414 patent is the same as claim 7, except broader in that it includes all phosphatases and not just ptpl1. Claim 6 anticipates claim 8, and claims 11-13 are anticipated by claims 9-11.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a method of identifying a modulator of NMDA receptor signaling activity comprising detecting the ability of an agent to modulate the phosphatase activity of a protein tyrosine phosphatase (PTP) "with NMDA-R on a substrate." The specification refers to 'substrates' as phosphatase or kinase ***targets***, such as SRC and FYN, and NMDA receptor itself. Therefore, it is not known what the meets and bounds of "with NMDA-R on a substrate" are. For purposes of art, the examiner interprets "with NMDA-R on a substrate" very broadly to mean 'attached to something.' Claims 2-5 are rejected as they depend from claim 1.

7. Claims 7-13 are rejected because it is not known what "a difference" at the end of claim 7 refers to. An increase or decrease in phosphorylation? Appropriate correction is required. Claims 8-13 are rejected as they depend from claim 7.

8. Claim 8 is rejected because the meets and bounds of 'a protein complex' are not known. Are NMDA receptors bound to a phosphatase, a phosphatase and a kinase, a multitude of proteins? The meets and bounds of 'a protein complex' are not known.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (1994).

Wang et al disclose detecting the ability of orthovanadate, a protein tyrosine phosphatase inhibitor, to modulate NMDA receptor activity (see figure 3, page 235). Therefore Wang et al discloses a method that identifies a modulator of NMDA receptor activity, by detecting the ability of an agent, orthovanadate, to modulate phosphatase activity of protein tyrosine phosphatases, which meets the limitations of claims 1. The NMDA receptors, in the case of Wang et al., are located on the synaptic plasma membrane, which is reasonably "with said NMDA-R on a substrate." Vanadate blocks tyrosine dephosphorylation of SRC (and SRC tyrosine-phosphorylates NMDA receptors; see below, and see Wang et al, figure 2D), and therefore inhibits a tyrosine phosphatase capable of dephosphorylating a kinase that phosphorylates NMDA receptors, meeting the limitations of claim 2. Wang et al use human SRC (see figure 2D, page 234), meeting the limitations of claim 3. Since orthovanadate is disclosed by Wang et al as a protein tyrosine phosphatase inhibitor (see first line of Figure 3), the effect on NMDA receptor current with and without orthovanadate is a direct measurement of tyrosine phosphatase activity. Therefore, Wang et al also meet the limitations of claim 5.

8. Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Grant (WO 97/46877; published December, 1997).

Grant discloses methods of identifying compounds that modulate tyrosine phosphatase activity comprising detecting the phosphorylation state of the NMDA receptor, and NMDA receptor signaling complex (NRSC), which contains tyrosine phosphatases and kinases (see front page, see figure 1-4, and see pages 12-14, starting at line 31 on page 12 and ending at line 5 of page 14). NRSC is comprised of the NMDA receptor NR1, NR2A and B, PSD-95, Fyn or SRC, and several different tyrosine phosphatase that are known to dephosphorylate SRC (see figure 1), thus meeting the limitations claims 1-3 and 5. lines 1-5 on page 14 disclose identifying agents that 'disrupt or alter the composition,' which reasonably meets the limitations of claim 6. On page 3, Grant discloses that the methods of identifying drugs are to use natural or artificial human NRSC complexes, thus meeting the limitations of claim 4. At the bottom of page 13 testing the action of compounds on the NRSC is also disclosed. Considering this, and the composition of the NRSC, which includes all the elements of I-iii of claim 7 and the measurements of the tyrosine phosphorylation of NR2A and B reported on page 13 (middle of top paragraph) in the presence and absence of a compound that stimulates NMDA receptor activation, Grant meets the limitations of claim 7-8. Grant is silent with regard to identifying agents that inhibit or enhance said phosphatases ability to dephosphorylate SRC kinase. However, since dephosphorylation of SRC causes SRC to become more active (and thereby phosphorylated NMDA receptor subunits to a greater degree), and because grant measures the tyrosine phosphorylation of all proteins in the NRSC, including the NMDA receptor substrates, the method of Grant works to identify the compounds with the

properties recited in claims 9-10. Lines 1-5 on page 14 disclose identifying agents that 'disrupt or alter the composition,' which reasonably means 'binding' as recited in claims 11-13.

Conclusion

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bagrodia et al discloses that orthovanadate inhibits tyrosine phosphatase mediated dephosphorylation of SRC Tyrosine 527, which causes SRC to be active (see abstract). Husi et al (2000) further discloses the content of the NRSC complex immunoprecipited from mouse brain using anti-NMDA-R1 antibodies (as performed by Grant above) as containing multiple attached kinases and phosphatases including PP1, PP2A, PTP1D (aka, SHP2), and SRC (see table 1, under 'phosphatases' and kinases). Roskoski (2005) discloses that phospho-SRC at Tyrosine 527 is a target for SHP2 tyrosine phosphatase (see abstract).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
4/26/06

LORRAINE SPECTOR
PRIMARY EXAMINER